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ABSTRACT OF THE DISCLOSURE

We report the use of telomerase-immortalized human microvascular endothelial cells in the formation of functional capillary blood vessels *in vivo*. Previously we showed the superior *in vitro* survival of human telomerase reverse transcriptase (hTERT)-transduced human endothelial cells. Here we show that retroviral-mediated transduction of hTERT in human dermal

10 microvascular endothelial cells (HDMEC) results in cell lines that form microvascular structures when subcutaneously implanted in severe combined immunodeficiency (SCID) mice. The human origin of xenografted microvaculature was confirmed both by basement membrane immunoreactivity with anti-human type IV collagen staining and visualization of fluorescent

15 vessels containing HDMEC that were co-transduced with hTERT and green fluorescent protein (eGFP). The lack of human vascular structures after implantation of HT1080 fibrosarcoma cells, 293 human embryonic kidney cells or human skin fibroblasts demonstrated the specificity of HDMEC at forming capillaries. Intravascular red fluorescent microspheres injected into the host

20 circulation were found within green "telomerized" microvessels indicating functional murine-human vessel anastomoses. Whereas primary HDMEC-derived vessel density decreased steadily with time, telomerized HDMEC maintained durable vessels 6 weeks after xenografting. Modulation of implant vessel density by exposure to different angiogenic and angiostatic factors demonstrated the utility of this system for the study of human microvascular remodeling *in vivo*.